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Increasing outpatient treatment of mild community-acquired pneumonia: systematic review and meta-analysis

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ABSTRACT: In order to identify, synthesise and interpret the evidence relating to strategies to increase the proportion of low-risk patients with community-acquired pneumonia treated in the community, we conducted a systematic review of intervention studies conducted between 1981–2010.

Articles were included if they compared strategies to increase outpatient care with usual care. Outcomes were: the proportion of patients treated as outpatients, mortality, hospital re-admissions, health related quality of life, return to usual activities and patient satisfaction with care.

The main analysis included six studies. The interventions in these studies were generally complex, but all involved the use of a severity score to identify low-risk patients. Overall, a significantly larger numbers of patients were treated in the community with these interventions (OR 2.31, 95% CI 2.03–2.63). The interventions appear safe, with no significant differences in mortality (OR 0.83, 95% CI 0.59–1.17), hospital readmissions (OR 1.08, 95% CI 0.82–1.42) or patient satisfaction with care (OR 1.21, 95% CI 0.97–1.49) between the intervention and control groups. There was insufficient data regarding quality of life or return to usual activities. All studies had significant limitations.

The available evidence suggests that interventions to increase the proportion of patients treated in the community are safe, effective and acceptable to patients.

KEYWORDS: Acute respiratory infection, community-acquired pneumonia, disease management, guidelines, guidelines for management of pneumonia, infections

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Community-acquired pneumonia (CAP) is the most common infectious disease presenting to emergency departments in western countries [1]. Population-based studies of CAP in Europe suggest an incidence of CAP requiring hospitalisation of 1.98–2.6 per 1,000 population per year [2, 3]. Approximately 75% of cases are managed in the community, where mortality is very low. The mortality rate in hospitalised patients is reported to be 5–15% [4, 5].

Treatment of CAP costs over 8 billion dollars annually in the USA [6]. More than 90% of that expenditure relates to the cost of in-patient care [6]. The initial decision, made by the attending physician, to admit the patient to hospital or discharge the patient from hospital is, therefore, crucial.

In recent years, severity assessment tools such as the Pneumonia Severity Index (PSI) and the CURB65 (new onset mental confusion, urea >7 mM, respiratory frequency $\geqslant$30 breaths·min^{-1}, systolic blood pressure <90 mmHg or diastolic blood pressure $\leqslant$60 mmHg, and age $\geqslant$65 yrs) score have been developed [4, 5]. These tools allow patients to be categorised into groups at low, intermediate and high risk for 30-day mortality. Patients at low risk for mortality are more likely to be suitable for outpatient care. These tools are now promoted by almost all national and international guidelines to aid clinicians in making the site-of-care decision [1].

Strategies to increase the proportion of patients treated in the community have the potential to significantly decrease hospital costs, but must be safe and acceptable to patients [7].

In this study, we systematically reviewed the published literature to identify, synthesise and

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interpret the evidence relating to strategies to increase the proportion of low-risk patients with CAP treated in the community.

The aim of the study was to establish if these interventions could increase the proportion of patients treated in the community without compromising patient satisfaction with care, healthy-related quality of life and return to usual activities, or increasing hospital readmissions or mortality.

METHODS

This was a systematic review and meta-analysis conducted and reported according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations [8].

Search strategy

The present review was based on a search of PubMed and EMBASE for articles using keywords ''outpatient'', ''discharge'', ''home'', ''hospitalisation/hospitalization'' or ''guideline'' in combination with ''community-acquired pneumonia'' was performed between January 1981 and April 2010. Nonrelevant studies were excluded based on title and abstract review only. Full articles of all potentially appropriate abstracts were retrieved and reviewed by investigators. No language restriction was applied. Only peer-reviewed data was included: therefore, conference abstracts were excluded. The search strategy was supplemented by reviewing of reference lists, bibliographies and the investigators' files.

Study inclusion criteria and quality assessment

Data was independently extracted from each relevant study by two abstractors and these abstractors carried out quality assessment using standardised criteria [9]. Quality assessments were performed separately and disagreements resolved by a third independent abstractor.

Studies were included if they met the following criteria: 1) original publication; 2) describe an intervention aimed to increase the proportion of patients treated in the community; 3) include a control group in which the intervention was withheld; and 4) include data reporting the safety of the intervention.

Studies reporting outpatient care but without control data were not included.

End-points

The primary outcome was the proportion of patients treated in the community in the intervention groups compared to the control groups. Measures of safety were also assessed as follows: mortality, readmission to hospital in community-treated patients, patient satisfaction with care, health-related quality of life, and return to work or usual activities.

Statistical analysis

Statistical analysis was performed using Review Manager, version 5 (Cochrane IMS, Oxford, UK). Pooled data are presented as OR (95% CI). A fixed-effects model was used to pool the results of individual studies. Heterogeneity of study results were assessed by calculating a Chi-squared test of heterogeneity and the I^2-test for inconsistency. Significant heterogeneity was predefined as a Chi-squared test $p<0.1$ or an I^2-test $>50\%$. Publication bias was assessed using the Funnel plot method.

RESULTS

The literature review identified six studies for inclusion in the meta-analysis [10–15]. Details of the literature review are shown in figure 1.

Details of each study are shown in table 1.

The interventions used in each study were generally complex, but all included a scoring system to identify low-risk patients. In five studies, the PSI was used to help determine where patients should be treated in the intervention arm. In one study, the authors derived their own criteria for in-patient care and then implemented this. No clinical trials using any of the other available severity scores were identified.

Description of included studies

In the study by ATLAS *et al.* [10], a single-centre intervention, the authors implemented a practice guideline for patients with low PSI scores. The study included patients with PSI scores I–III and excluded patients with significant hypoxaemia, patients with immunosuppression, injecting drug users and patients with other co-morbidities that were considered a contra-indication to outpatient care. The intervention involved promoting the use of the PSI in the emergency department and supporting discharge by providing nursing visits at home, standardised antibiotic treatment (clarithromycin monotherapy) and access to a primary care physician. Care after the intervention was compared to a retrospective control cohort identified from case-note review. Significantly more patients were treated as outpatient in the intervention compared with the control cohort [10].

In the study by MARRIE *et al.* [11], the intervention was the implementation of the critical pathway composed of three parts: 1) promoting the use of the PSI; 2) treatment with levofloxacin; and 3) implementation of a practice guideline that included standard microbiological tests, *i.v.*-to-oral switch criteria and hospital discharge criteria. Nine hospitals implemented this critical pathway while 10 hospitals managed patients according to their usual practice. This did not include pneumonia severity scoring or the other components of the critical pathway [11].

In the study by DEAN *et al.* [12], a clinical practice guideline based on the American Thoracic Society guidelines was

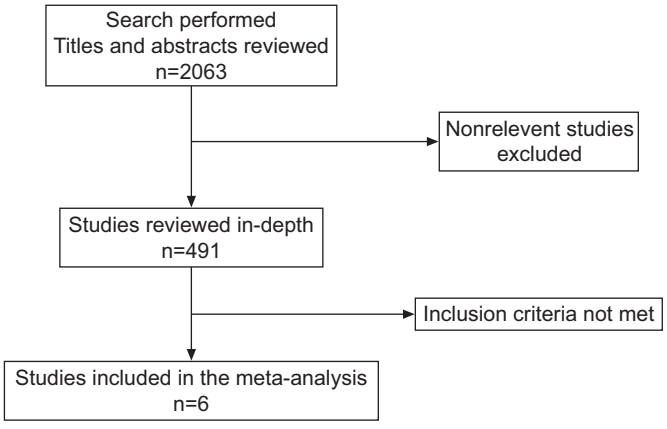

FIGURE 1. Process of literature review.

TABLE 1 Characteristics of included studies

First author [ref.]	Year of publication	Setting	Design	Group 1 (n)	Group 2 (n)	Patients treated in the community# %	Readmission# %	Mortality# %
Atlas [10]	1998	Single emergency department, Boston, MA, USA	Prospective intervention with retrospective control group	Implementation of PSI-based guideline (166)	Retrospective control group prior to the intervention (147)	56.6/41.5	4.8/0	0/0
Marrie TJ [11]	2000	19 emergency departments, Canada	Implementation of a critical pathway with control hospitals	Critical pathway hospitals (716)	Conventional management (1027)	69/51	0.7% increase in readmissions in group 1	0.1% higher in group 2
Dean [12]	2000	4 walk-in medical centres, Salt Lake City, UT, USA	Implementation of a practice guideline with retrospective controls	Pneumonia practice guideline including-site-of care decision support (264)	Retrospective control cohort using conventional management (199)	93.6/86.4	1.1/2.5	0/1
Carratala [13]	2005	2 emergency departments, Barcelona, Spain	Randomised controlled trial of outpatient *versus* in-patient management	Outpatient management (109)	In-patient management (114)	NA	6.3/7.0	0.9/0
Yealy [14]	2005	32 emergency departments, Pennsylvania and Connecticut, USA	Implementation of PSI-based guidelines at low, moderate and high intensity	Moderate- and high-intensity implementation of guidelines (1456)	Low-intensity guideline implementation (445)	61.4/37.5	5.9/6.6	1.4/2.3
Renaud [15]	2007	16 emergency departments, France	Prospective observational study with control hospitals	Emergency departments using the PSI (215)	Emergency departments not using the PSI (234)	42.8/23.9	1.6/0.6	0.5/2.6

PSI: Pneumonia Severity Index; NA: not applicable. #: group 1/group 2, unless otherwise stated.

introduced. The guideline included a decision support system to determine site of care that included a scoring system. This study is unique in not using the PSI to determine initial site of care; instead, the authors determined their own criteria for outpatient care and incorporated these into the guideline. The study is also unique as it took place in community-based walk-in medical centres rather than emergency departments, as was the case in the other studies. Data for 12 months after the introduction of the guideline were compared to a retrospective control group of patients treated before implementation of the guideline [12].

In the study by Carratala *et al.* [13], patients were randomised to out- *versus* in-patient management. Outpatients were treated with oral levofloxacin and in-patients treated with sequential *i.v.* then oral levofloxacin. Patients were excluded if they were intolerant of quinolones, were pregnant or breast feeding, or had respiratory failure, unstable comorbidities, pneumonia complications (pleural effusion or lung abscess), or were unable to take oral medications [13]. Outcomes were determined 30 days after randomisation and included mortality, the number of readmissions, and adverse drug reactions and patient satisfaction with care.

Yealy *et al.* [14] conducted as cluster-randomised trial at 32 emergency departments in Pennsylvania and Connecticut, USA. Centres were randomised to one of three intensities of pneumonia guideline implementation. The intervention included instructions to use the PSI, and to manage patients in class I–III without oxygen desaturation as outpatients. The guideline also suggested administration of antibiotics for inpatients within 4 h and recommended appropriate empirical antibiotic therapy. The low-intensity strategy simply involved writing to medical directors of hospitals suggesting that they develop pneumonia quality improvement strategies and mailing the emergency department with the guideline. The moderate- and high-intensity strategies included the measures for the low-intensity group but also an on-site teaching session on how to use the PSI and encouragement of outpatient treatment. The high-intensity group also included a number of additional reminders and feedback systems [14].

In the study by Renaud *et al.* [15], an observational study, eight emergency departments in which the PSI was used to determine site of care were compared with eight emergency departments in which the PSI was not used. PSI-using hospitals were provided with posters and pocket cards reminding them to use the PSI, while control hospitals were not. No other interventions were used. Each hospital completed data collection for 3–5 months and the primary outcome was the proportion of patients discharged from the emergency department [15].

The results of these studies are summarised in table 1.

Outpatient management using clinical guidelines

We included five studies in the meta-analysis for outpatient care. The study by Carratala *et al.* [13] was unique in randomising all patients to out- or in-patient treatment rather than implementing a clinical guideline to increase the proportion of patients treated in the community; therefore, this was not included in this part of the analysis. The definition of outpatient treatment was only specifically given

in the study by YEALY *et al.* [14], defined as discharge from the emergency department to the community within 24 h. In the other studies, outpatient treatment was assumed to meet the same definition.

The analysis included a total of 2,817 patients in the intervention groups and 2,052 patients in the control groups. In raw analysis, 64.6% of patients in the intervention group were treated in the community compared with 48.7% of patients in the control groups.

In the meta-analysis, the interventions were associated with a significant increase in outpatient-managed patients (OR 2.31, 95% CI 2.03–2.63). The Forest plot is shown in figure 2. There was no significant heterogeneity.

Safety of the intervention

For the two measures of safety, mortality was not increased (OR 0.83, 0.59–1.17) (fig. 3).

For hospital readmissions, the studies by ATLAS *et al.* [10], DEAN *et al.* [12], YEALY *et al.* [14] and RENAUD *et al.* [15] reported readmissions only for patients initially treated in the community in both intervention and control groups. The definition of readmission was unclear in the study by MARRIE *et al.* [11]. CARRATALA *et al.* [13] compared readmissions in patients discharged from the emergency department to those patients initially hospitalised and then subsequently discharged.

Separately, none of these studies showed an increase in hospital readmissions. Similarly, the pooled analysis showed no increase in hospital readmissions (OR 1.08, 95% CI 0.82–1.42; fig. 4). There was no significant heterogeneity in these analyses.

Patient satisfaction with care

Only three studies reported data for patient satisfaction with care between intervention and control groups. In the studies by CARRATALA *et al.* [13] and ATLAS *et al.* [10], patients were asked to rate their satisfaction with care at 4 weeks on a scale of 1–5 (very unsatisfactory to very satisfactory) with 4 or 5 considered satisfied. In the study by YEALY *et al.* [14], telephone interviews were conducted at day 30 and patients were asked if they were satisfied with their initial site of care, their emergency department care and their overall medical care.

Pooling the results of the three studies, there was no difference between the intervention and control groups (OR 1.21, 95% CI 0.97–1.49; p=0.09) in the proportion of patients reporting satisfaction with overall care. There was no significant heterogeneity in the analysis (fig. 5). This conclusion was based predominantly on the results of the study by YEALY *et al.* [14], which was significantly larger than the other two studies.

Return to usual activities and quality of life

There were insufficient data to pool studies of return to usual activities or quality of life. ATLAS *et al.* [10] reported return to daily activities, with 92% of patients in the intervention and 85% in the retrospective control group reporting return to usual activities (p>0.05). They also reported no difference in patients reporting general health excellent or very good at 4 weeks.

The study by MARRIE *et al.* [11] reported quality of life using the Short-Form 36 physicial component summary scale (SF-36) and reported no significant difference between intervention and control hospitals. CARRATALA *et al.* [13] also assessed health-related quality of life using the SF-36 tool and found no significant difference at day 7 or day 30 in health-related quality of life between patients managed as in-patients or outpatients. YEALY *et al.* [14] assessed return to work and usual activities at day 30 and found no significant differences in these parameters between the low-, moderate- and high-intensity guideline implementation groups. Finally, RENAUD *et al.* [15] and DEAN *et al.* [12] did not assess return to usual activities or quality of life.

Publication bias

In each of the analyses, inspection of funnel plots did not suggest any evidence of publication bias (data not shown).

Quality assessment

Each of the included studies had significant limitations. The studies by ATLAS *et al.* [10] and DEAN *et al.* [12] utilised a retrospective control cohort design, a method associated with a significant risk of bias. Similarly, the centres included in the study by RENAUD *et al.* [15] were not randomised. Instead, the study included hospitals that had decided independently to

First author [ref.]	Intervention		Control		Weight %	OR (95% CI)	Year
	Events n	Total n	Events n	Total n			
ATLAS [10]	94	166	61	147	9.2	1.84 (1.17–2.88)	1998
DEAN [12]	247	264	172	199	4.2	2.28 (1.21–4.31)	2000
MARRIE [11]	494	716	524	1027	44.0	2.14 (1.75–2.61)	2000
YEALY [14]	894	1456	167	445	32.5	2.65 (2.13–3.30)	2005
RENAUD [15]	92	215	56	234	10.1	2.38 (1.59–3.56)	2007
Total	**1821**	**2817**	**980**	**2052**	**100.0**	**2.31 (2.03–2.63)**	

Heterogeneity: Chi-squared=3.08, df=4 (p=0.54); I^2=0%
Test for overall effect: Z=12.62 (p<0.00001)

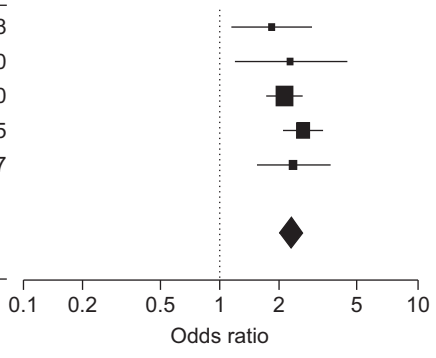

FIGURE 2. Forest plot. Proportion of patients treated in the community in the intervention and control cohorts. Events: patients treated in the community in each group. Odds ratio from Maentel–Hentzel fixed-effects model. Whiskers represent 95% confidence interval. df: degrees of freedom.

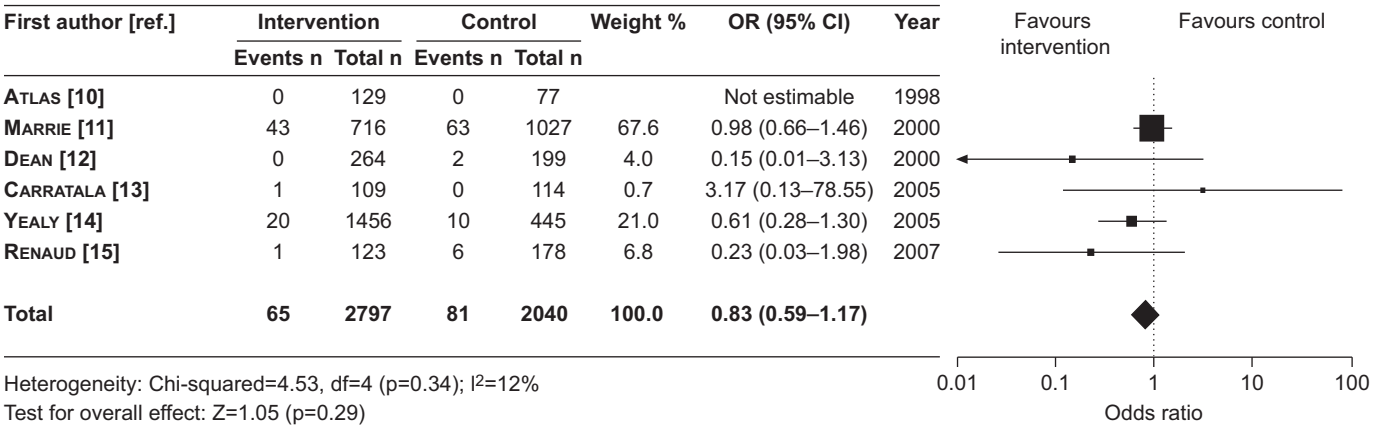

FIGURE 3. Forest plot. Mortality among low-risk patients in the intervention and control cohorts following implementation of measures to increase outpatient management. Events: deaths in each group. Odds ratio from Maentel–Hentzel fixed-effects model. Whiskers represent 95% confidence interval. df: degrees of freedom.

implement the PSI and control hospitals that had not. There is no way of knowing to what extent other aspects of CAP management were different in these centres, or that the PSI was not used in the control hospitals. The cluster randomisation design utilised in the studies by MARRIE *et al.* [11] and YEALY *et al.* [14] are more robust; however, as the PSI is a well known and widely used instrument, randomisation at the hospital level cannot ensure the intended practice at the individual-physician level. The study by CARRATALA *et al.* [13] was more robust, as a randomised controlled trial in two centres but was underpowered to detect mortality, which is rare in low-risk patients. The study also had to exclude a large proportion of patients as many otherwise low-risk patients are not suitable for outpatient care. All of the guideline interventions were composed of multiple components and, therefore, evaluating which of these components were responsible for the effects seen is not straightforward.

DISCUSSION

This systematic review and meta-analysis demonstrates that, based on the available evidence, strategies to increase the proportion of patients treated in the community are safe, effective and acceptable to patients. Increased use of outpatient care for low-risk patients, primarily defined using the PSI, was associated with no significant increase in hospital readmissions, patient mortality or patient dissatisfaction with care [10–15]. There were limited data on other safety outcomes, such as health-related quality of life and return to usual activities.

Each of the six included studies had significant limitations and each used a variety of different methods to encourage outpatient management. All of these studies, however, were based on the principle that patients at low risk of death and without important contraindications to outpatient treatment, such as inability to take oral medication or unstable comorbidities, can be treated safely at home. The studies were conducted in the USA, Canada, France and Spain, suggesting that these results can be generalised to different healthcare systems [10–15].

The PSI was developed in 1997 with the aim of identifying a population of patients at low risk for mortality who may be suitable for outpatient therapy [4]. This score has been shown to be reliable in a large number of validation studies [16–20]. Evidence suggests that since the introduction of PSI, the length of stay for patients with CAP may have decreased and more patients may be initially treated in the community [21]. There is,

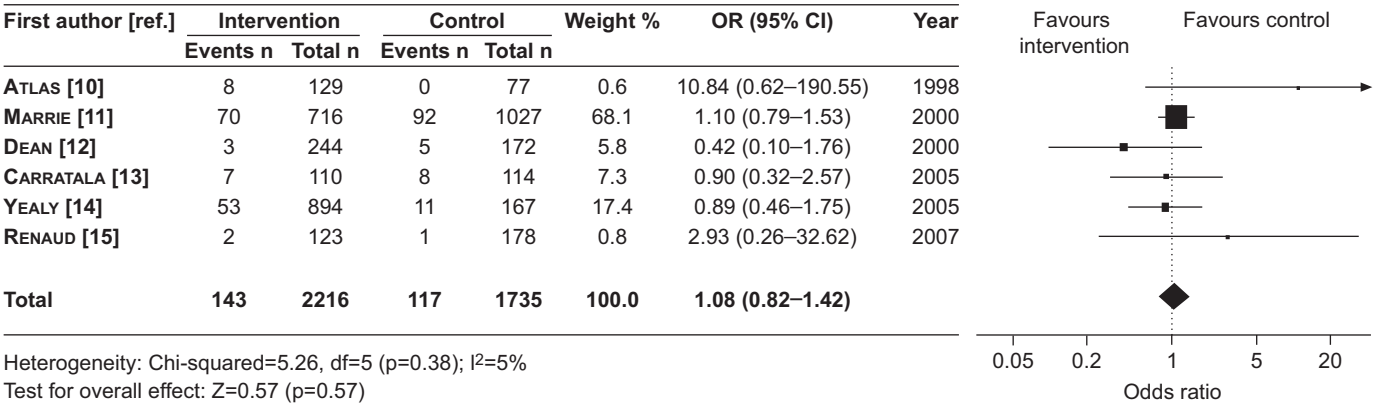

FIGURE 4. Forest plot. Readmissions following hospital discharge in the intervention and control cohorts. Events: readmissions following hospital discharge. Odds ratio from Maentel–Hentzel fixed-effects model. Whiskers represent 95% confidence interval. df: degrees of freedom.

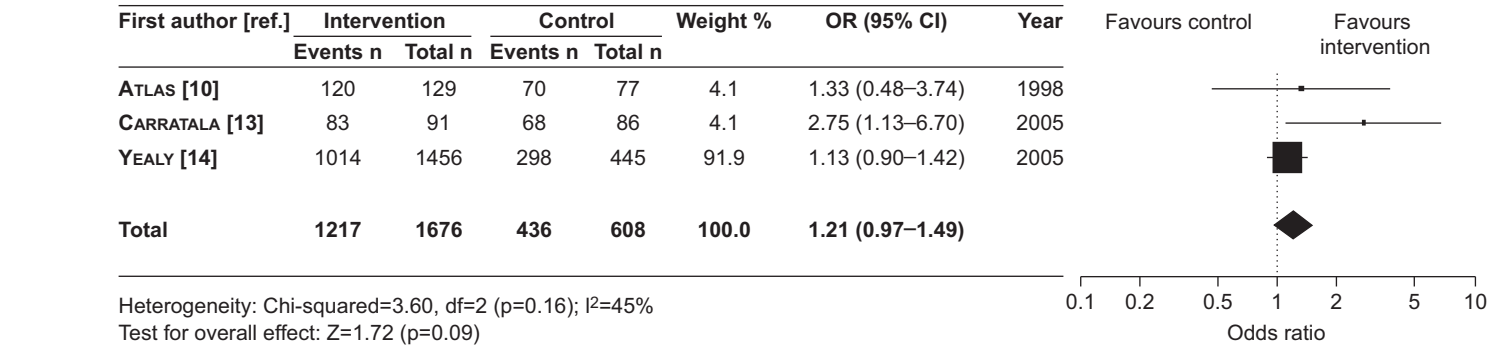

FIGURE 5. Forest plot. Satisfaction with care in the intervention and control cohorts following implementation of measures to increase outpatient management. Events: patients reporting satisfaction with care. Odds ratio from Maentel–Hentzel fixed-effects model. Whiskers represent 95% confidence interval. df: degrees of freedom.

however, evidence from a number of studies, including those included in this meta-analysis, that a larger proportion of patients could be safely treated in the community [10–15].

Outpatient management has several potential advantages. More than 90% of hospital costs are associated with in-patient care and even small increases in the proportion of patients treated at home can result in large economic savings [6, 22]. Hospital-acquired infections, such as methicillin-resistant *Staphylococcus aureus* and *Clostridium difficile*, are an increasing problem in the UK and internationally [23, 24]. Reducing the proportion of patients treated in hospital will reduce the risk of patients developing these hospital complications.

Barriers to outpatient treatment

All of the quality improvement studies found a proportion of low-risk patients still requiring inpatient treatment. Physician judgement is critical in the implementation of severity scores [25]. A number of studies have investigated reasons why low-risk patients require hospitalisation and show that comorbid illnesses, inability to take oral medications, severity not adequately captured by the PSI and hypoxaemia are frequent in low-risk patients [25, 26]. These factors must be taken into consideration when implementing outpatient management strategies.

Evidence suggests that physicians overestimate the severity of low-risk patients [26]. It is notable that each of the successful quality improvement studies in this meta-analysis included some degree of physician education and feedback. This is well demonstrated in the study by YEALY *et al.* [14], in which low-intensity implementation of guidelines, in which physicians were simply provided with the guidelines, were significantly less effective than the moderate-/high-intensity group, in which guidelines were supplemented with physician education and feedback. There is evidence that the PSI and other severity assessment tools are under-utilised in some centres [27].

This study did not identify any clinical studies or trials of severity scores other than the PSI and a site-specific score developed by DEAN *et al.* [12] to increase the proportion of patients treated in the community. It is uncertain if the results of this meta-analysis can be generalised to other methods or scoring systems [5, 28, 29].

Limitations of the included studies

As discussed above, potential bias must be considered in interpreting these results. Although the meta-analysis found no indication of publication bias, the methodology of each study varied substantially. The studies by ATLAS *et al.* [10] and DEAN *et al.* [12] used retrospective control cohorts. When different methodologies are used to collect data for the intervention and control groups, the risk of bias is increased. The analysis of patient satisfaction with care was largely based on a single study (YEALY *et al.* [14]) and, therefore, further studies on this end-point would be desirable. This meta-analysis was an aggregate meta-analysis rather than an individual patient data-level analysis. The latter offers several advantages [30] and the use of aggregate methods in this study is a limitation. The pooled results should be treated with caution as, although there was no statistical heterogeneity, there were differences between studies in the interventions used and the characteristics of the healthcare systems in which they were implemented.

Implementation and future studies

The results of this meta-analysis suggest that emergency departments should be encouraged to develop strategies to manage more patients in the community, using validated criteria to ensure these interventions are safe. Further interventional studies are required, particularly with respect to severity criteria other than the PSI that have not yet been tested for guiding outpatient management. Limited data are available for important end-points, such as health-related quality of life, symptom resolution, and return to work and usual activities, and further studies in this area are needed.

Conclusion

Current evidence suggests that strategies to increase the proportion of patients treated in the community are safe, effective and acceptable to patients.

SUPPORT STATEMENT

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STATEMENT OF INTEREST

None declared.

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